PATENT
Docket No. GC507-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application:	
Becker *et al.*	Group Art Unit: 1631
Serial No.: 09/215,095	Examiner: Borin, M. L.
Filed: December 18, 1998	
For: Matrix Granule	

APPELLANT'S BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This appeal is from the decision of the Examiner dated July 22, 2003, finally rejecting claims 66-69, 72-76 and 78-100, which are reproduced as Appendix I to this brief. A Notice of Appeal for this final rejection was filed for this application on August 27, 2003, and a 3 month extension of time to file this Appeal Brief accompanies this response.

The Commissioner is authorized to charge any fees that may be required by this paper to Deposit Account No. 07-1048.

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1. REAL PARTY IN INTEREST

The real party of interest in this application is Genencor International, Inc. assignee of the entire right, title and interest to this application by virtue of an assignment from Nathaniel T. Becker, Thomas S. Green, and Robert I. Christensen, Jr.

2. STATEMENT OF RELATED CASES

There are no other appeals and/or interferences related to the appeal taken in this application.

3. STATUS OF THE CLAIMS

Claims 66-69, 72-76 and 78-107 remain in this application with Claims 70, 71, and 77 having been cancelled. Claims 66-69, 72-76 and 78-107 stand finally rejected under 35 USC § 103 as being unpatentable over Arnold et al. US Patent No. 5,324,649 in combination with US Pat. No. 5,254,287 or US Pat. No. 5,260,074.

4. STATUS OF THE AMENDMENTS

A final Office Action was mailed on April 30, 2003, and a response was mailed on June 30, 2003, amending claims 66, 67, 74, 83, 87, 88, 101, 106 and 107. An Advisory Action was mailed on July 22, 2003, rejecting all claims and advising that the June 30, 2003, amendment will be entered into the application upon filing of an Appeal Brief. No other amendments have been requested for entry into this application subsequent to the Advisory Action. Accordingly, the listing of the claims on appeal as set forth in the attached Appendix I reflect the amendments requested with the Response to the Final Office action.

5. SUMMARY OF THE INVENTION

The presently claimed invention is in general directed to particles or granules having a protein component for use particularly in detergents and the cleaning industry. In one embodiment, the granule comprises a single seed particle layered over with a protein matrix which comprises a protein solution or slurry to which is added a

combination of a sugar or sugar alcohol and a polysaccharide structuring agent, and an outer barrier layer of coating. (See, Specification: Page 5, lines 24-30; page 6, lines 19-31; and Examples).

In another embodiment, the layers of a granule having a single seed particle comprise an enzyme matrix that is 20-80% by weight of the granule and comprises an enzyme solution or slurry mixed together with an added combination of a sugar and polysaccharide structuring agent, and an outer barrier or coating. In this embodiment the enzyme of the solution or slurry is selected from proteases, amylases, lipases and cellulases, and the structuring agent is selected from starch, modified starch, cellulose, modified cellulose, carrageenan, gum Arabic, xanthAn gum, locust bean gum, and guar gum. (See, Specification: Page 7, lines 6-7; page 8, lines 20-25; and page 8, lines 31 through page 9, line 8).

In yet another embodiment, the granule is a single seed particle layer over with an enzyme matrix (20 to 80% be weight of the granule) which includes at least one enzyme solution or slurry mixed together with an added combination of a sugar and at least one polysaccharide structuring agent. In this embodiment, the granule has a barrier salt over the enzyme matrix layer and an outer coating over the barrier layer. (See, Specification: Page 8, lines 20-25).

The specification and claims describe, in detail, such compositions at from page 5, line 17, to page 9, line 8; and the Examples.

6. STATEMENT OF ISSUES FOR REVIEW

The sole issue for consideration by the Board of Appeals and Patent Interferences is as follows:

is the rejection of claims 66-69, 72-76 and 78-107 under U.S.C. § 103 over Arnold et al. US Patent No. 5,324,649 in combination with US Pat. No. 5,254,287 or US Pat. No. 5,260,074 proper?

7. GROUPING OF CLAIMS

All of the appealed claims will be grouped together for the purpose of Appellants' argument.

8. ARGUMENTS AND CONCLUSION

Background

In order to facilitate understanding of Appellants' argument for the above issues, Appellants will first discuss the basis of the present invention in more detail than that set forth in Paragraph 5 above.

Appellants' claimed invention is directed to granules having a seed particle layered over with a protein matrix to which is added a combination of a sugar or sugar alcohol and a polysaccharide structuring agent, and an barrier or outer coating layer. Accordingly, the claims covering this invention are composition claims.

Proteins, including enzymes, must be stabilized when stored in harsh cleaning compounds to prevent loss of enzyme activity, and one method of protection is to form a particle made up of the protein and components that stabilize the protein. The particles should both stabilize and maintain protein activity as well as protect against the release of protein (enzyme) dust into the atmosphere because such dust can sensitize and result in allergic reactions. Most important, the protein must be available and able to perform its function when the cleaning compound is in use, such as, for example, when a detergent with enzyme granules is added to wash water.

Several types of particles are used in the industry. One type typically mixes the protein into other components of the particle to form a homogeneous composition, and the particle may include protective coatings over the composition. Another type claimed by Appellants places the protein in one or more layers around a core particle with protective coatings over the protein layer.

Appellants' granule is made from a seed particle and a matrix surrounding the seed particle. The matrix includes a protein (or enzyme) solution or slurry mixed together with a combination of a sugar or sugar alcohol and a polysaccharide structuring agent. In one preferred embodiment, as exemplified in Example 2, the seed particle is sodium sulfate crystals and the matrix is a mixture of a protease enzyme solution in combination with sucrose and starch. The granule is further coated with one or more coatings including methylcellulose, titanium dioxide, Neodol and PEG.

As taught in Appellants' disclosure at page 7, Appellants discovered the advantage of mixing the protein solution or slurry with sugar and polysaccharide structuring agent to form an admixture that protects the protein from activity loss and attrition. The advantage is unexpected because sugar is known to have

disadvantageous "binder" characteristics that make granules sticky. At page 7(lines 8-13), it is stated,

> "By burying a protein within a matrix, the protein can be better protected from the twin dangers of attrition and activity loss. However it has not been possible previously to granulate enzymes in sugar or sugar alcohol matrices, since sugars and sugar alcohols exhibit "binder" characteristics, i.e. they are sticky and tend to plaster particles together (as happens intentionally in the case of granulation by agglomeration)."

Also as stated at page 7,

> "Surprisingly, it has been found that by the addition of a structuring agent to the sugar matrix formula, protein can be applied uniformly to individual seed particles at rapid rates without agglomeration or attrition."

The structuring agents, polysaccharides, typically have an anti-tack characteristic which is helpful in reducing the binder characteristic of the sugar or sugar alcohol, and allows the matrix to be built up, for example in fluid-bed coating at rapid rates without agglomeration. (see page 8).

General Argument as to Claims 66-69, 72-76 and 78-107

Appellants maintain, for the reasons set out below, that the rejection of Claims 66-69, 72-76 and 78-107 under U.S.C. § 103 over Arnold et al. US Patent No. 5,324,649 in combination with US Pat. No. 5,254,287 or US Pat. No. 5,260,074 is in error because there is no motivation to combine the cited reference in the manner of the claimed invention.

A *prima facie* case of obviousness requires the Examiner to cite to a reference or a combination of references which (a) suggests or motivates one of skill in the art to modify the teachings of the reference(s) to yield the claimed invention, (b) discloses the elements of the claimed invention, **and** (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish **any** one of these requirements precludes a finding of a *prima facie* case of obviousness.

"It is insufficient that the prior art disclosed the components of the patented device, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by the inventor." *Northern Telecom v. Data point corp.*, 908 F.2d 931, 934.

Thus, in order to establish a *prima facie* case of obviousness the USPTO must

show some objective teaching in the prior art or that knowledge generally available to one skilled in the art would lead that individual to combine the relevant teachings of the references. *In re fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). To invalidate claimed subject matter for obviousness, the combined teachings of the prior art references must suggest, expressly or by implication, the improvements embodied by the invention. Appellants contend that the selection of the combination suggested by the invention. *In re GPAC*, 35 USPQ2d 1116 (Fed. Cir. 1995) (citing *In re Sernaker*, 702 F. 2d 989, 217 *USPQ 1 (Fed. Cir. 1983).* The teachings of references can be combined only if there is some suggestion or incentive to do so.

Based on the above criteria, Appellants maintain that the cited prior art references, either alone or in combination, fail to achieve a *prima facie* case of obviousness against their claimed compositions.

Specifically, the Examiner and Appellants agree that a polysaccharide structuring agent, including starch, is a missing component in the enzyme layer of the granules of Arnold et al. US Pat. NO. 5,324,649. Arnold et al. teach the discovery of the protective nature of vinyl polymers used in the enzyme layer of a granule as well as in other locations of the granule, including the outer coating.

Arnold et al. describe the enzyme component of the granule as a conventional enzyme slurry or conventional "fermentation broth", which "typically include other proteins, peptide, carbohydrates, other organic molecules and salts". Col. 5, lines 32-37. The enzyme fermentation broth or slurry is then combined with a vinyl polymer or vinyl copolymer, such as PVA, with reduced water solubility in the case of fully hydrolyzed PVA, as described in Col. 5-6 of Arnold el al. This mixture of PVA and fermentation broth/slurry is used to coat a core in all of the examples in Arnold et al.

The granules in Arnold et al., particularly those in Example 5, are representative of the prior art granules used for comparison purposes in Appellants' specification, specifically, Example 1 which is the layered granule with a layer of enzyme and PVA referred to in Tables 1 and 4. As can be seen in Table 1, the matrix granule of the present invention demonstrated greater stability and lower Huebach dust values than that of the layered granule with the enzyme PVA layer. Table 4 also shows that the stability of the layered granule with the enzyme PVA layer is much less than that of the matrix granule of the present invention with the protein/sugar/polysaccharide layer. (See, Specification Table 4, Matrix Lot J.)

Optional ingredients may be added to the enzyme layer in Arnold et al. and include plasticizers (polyols such as sugars, sugar alcohols or polyethylene glycols having a molecular weight of less than 1000, ureas, or other known plasticizers such as dibutyl or dimethyl phthalate, or water) or anti-agglomeration agents (fine insoluble material such as talc, TiO2, clays and amorphous silica). (See Col. 6, lines 10-18).

Col. 2, lines 40-45 states that a preferred embodiment of the enzyme layer is "a PVA either alone or in combination with additional agents such as plasticizers or anti-agglomeration agents". No particular advantage is recited for any of the particular plasticizers and anti-agglomeration agents. None of the examples appear to include any of these optional agents in the enzyme layer.

Arnold et al. further includes a list of optional, adjunct ingredients that may be added to the granule (as opposed to added to the enzyme component) in Arnold et al. (Col. 7, lines 48-65), and that list also does not include polysaccharide structuring agents, including starch. Arnold et al. does not specify how or where to add such optional, adjunct ingredients to the granule. Specifically, the adjunct ingredients "may include metallic salts, solubilizers, activators, anti-oxidants, dyes, inhibitors, binders, fragrances, enzyme protecting agents/scavengers such as "ammonium sulfate, ammonium citrate, urea, guanidine hydrochloride, guanidine carbonate, guanidine sulfanate, thiourea dioxide, methylanolamine, diethanolamine, triethanolamine, amino acids such as glycine, sodium glutamate and the like, proteins such as bovine serum albumin, casein and the like, etc., surfactants, including anionic surfactants, ampholytic surfactants, nonionic surfactants, cationic surfactants and the long-chain fatty acid salts, builders, alkalis or inorganic electrolytes, bleaching agents, bluing agents and fluorescent dyes, and caking inhibitors". (See, Col. 7, lines 50-63).

Arnold et al. do not teach: amounts of adjunct ingredients, advantages of any particular adjunct ingredient, or combinations of any adjunct ingredients. It is clear that both the list of adjunct ingredients that can be added to the enzyme layer and the list of adjunct ingredients that can be added to the granule in general are non-specific teachings that do not lead to a matrix layer of a protein solution or slurry to which is added a combination of a sugar alcohol and a polysaccharide structuring agent.

Notwithstanding the statements in the Advisory Action to the contrary, the Arnold et al. Col. 7, lines 48-65 teaching would not provide any motivation to the skilled artisan to use a layer made of polysaccharide structuring agent mixed together with a sugar or sugar alcohol added to a protein solution or slurry to form a matrix for the protein.

Appellants contend that the teaching in Arnold et al. is a general teaching that, under the circumstances of this appeal, does not rise to the level necessary to satisfy the requirements of an obviousness rejection under 35USC § 103, in that it does not suggest, expressly or by implication, the claimed combination, nor does it provide any motivation for the claimed combination.

Properly considering the Arnold et al. reference as a whole, including the examples, leads to a granule having an inert core with or without a vinyl polymer coating, a layer of enzyme fermentation broth or slurry together with a vinyl polymer, an optional salt layer with or without vinyl polymer over the enzyme layer, and a final protective coating layer (for example, TiO2, PVA). The enzyme layer may further contain an optional plasticizer or anti-agglomeration agent. The rejection based on the primary reference appears to be based upon the optional ingredients in that reference.

Despite the assertions in the Advisory action, there is no motivation to look to the newly cited secondary references, US 5,254,287 and US 5,260,074 patents, without some teaching of particular benefits to the use of particular stabilizers. These secondary references relied upon in the rejection of Appellants' claims fail to cure the deficiencies of the Arnold et al. reference because both references do not employ a coating that has a protein matrix that comprises a protein solution or slurry to which is added a combination of a sugar or sugar alcohol and a polysaccharide structuring agent.

Specifically, US Pat. No. 5,260,074 to Sipos is for a digestive particle that solves the problem of friable granules composed of enzyme/salts of ursodeoxycholic acid (UDCA) and the problems caused by the presence of UDCA in digestive particles. The solution was to convert the UDCA to a pharmaceutically acceptable salt and add a buffer to preserve enzyme and UDCA activity. (See, Col. 3, lines 54 through Col. 4, lines 14). The buffering agent is selected from sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate and ammonium carbonate and from about 0.25 to about 1.5% tromethamine, diethanolamine and triethanolamine. (See, Col. 5, lines 31-37). The particles are not layered granules, but rather consist of a mixture of enzyme, buffering agent, a disintegrant (starch and modified starches, microcrystalliine cellulose and propylene glycol alginate), and an adhesive polymer. The mixture is then coated with an acid-resistant polymer. (See, Col. 5, lines 21-53). Sipos does mention in the background section of the patent that a prior art reference used enzyme stabilizers were selected from the group consisting of calcium carbonate,

polyvinylpyrrolidone, cellulose acetate phthalate, methylcellulose, starch and modified starches and alginic acid. The stabilizer was used in conjunction with an enzyme concentrate in a binder (sugars and sugar alcohols are not mentioned), and a disintegrant.

US Pat. 5,254,287 to Deleeuw et al. stabilizes enzymes for use in a bleach environment using the following protective agents: alkaline materials (sodium silicate and sodium carbonate); reducing materials (sodium sulfite and sodium thiosulfate; antioxidants such as BHT (buylated hydroxytolues or hydroxyanisole); transition metals (cobalt, nickel, copper).

While Deleeuw et al. and Sipos mention that starch can be an enzyme stabilizer, neither use starch as a stabilizer in their granules as solutions to the problems addressed in both references. As stated above, the Examiner agrees that the primary reference does not utilize or mention starch. Yet the Examiner contends that one skilled in the art would look to the Arnold et al. two different lists of adjunct ingredients and somehow select triethanolamine as a structuring agent from amongst a list of at least 10 protective agents, then look to Sipos or Deleeuw et al. - both of which use teach completely different protective materials - and decide to substitute starch for triethanolamine. Such a huge leap can only be accomplished using hindsight construction and is not taught or suggested in any of the references, either alone or taken together.

Further, even if the skilled in the art person finally selected starch for addition to the Arnold et al. granule, the sugar component might not be present since it also is only one of a list of optional ingredients. Even if the unlikely selection of a sugar plasticizer were to be added and a starch from the '287 or '074 patent were to be added, there still is no teaching to combine the sugar and polysaccharide with the protein to form a matrix layer of a granule as claimed by Appellants. In any selection of ingredients, the main protective agent in the enzyme layer would be the vinyl polymer.

Appellants' combination is not fairly suggested in the prior art, the rejections are based on impermissibly picking and choosing ingredients without considering the inventions as a whole, and the rejection looks suspiciously like hindsight reconstruction reached through the teachings of Appellants' disclosure. At best, the analysis is obvious to try. This is an improper basis for obviousness. The "obvious to try" standard has

been thoroughly discredited. Indeed, an obviousness rejection is inappropriate, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful" (quoting *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 [Fed. Cir. 1988], *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 10 USPQ2d 1843, 1845 [Fed. Cir. 1989]).

Appellants contend that an obviousness rejection must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, all of the facts must be considered, and the Examiner must supply the factual basis for the rejection. The Examiner may not, because he doubts that the invention is patentable, resort to speculation, unfounded assumptions, or hindsight reconstruction to supply deficiencies in the factual basis for the rejection. *See*, *In re Warner*, 379 F.2d 1011, 154 USPQ 173 (CCPA 1967). Furthermore, as stated by the Federal Circuit, (*W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 [Fed. Cir. 1983]):

> To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Finally, a fundamental requisite of establishing a *prima facie* case of obviousness is that there is a reasonable expectation of success in practicing the recited method steps or producing the claimed composition, without the use of the pending Application. Indeed,

> "[t]he reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."[1]

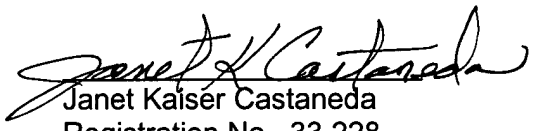
Furthermore, "routine experimentation" or something that is "routine in the art" does not negate patentability. (*See*, *in re Fay*, 347 F.2d 597, 146 USPQ 47, 51 (CCPA 1965); 35 U.S.C. § 103(a) ["Patentability shall not be negatived by the manner in which the invention was made"]). Thus, even if "routine experimentation" would lead one of ordinary skill in the art to produce the presently claimed compositions and methods, such a rejection would be improper. Under the law, an Examiner is **not** "one skilled in the art." (*See*, *Stratoflex, Inc., v. Aeroquip Corp.*, 218 USPQ 871, 879 [Fed. Cir. 1983]).

Consequently, the Examiner's own views regarding the obviousness of the presently claimed compositions and methods cannot enter into the determination of obviousness.

In view of the above, Appellants respectfully submit that the rejection of Claims 66-69, 72-76 and 78-107 is in error and, accordingly, request that the Board of Appeals reverse this rejection as set forth above.

Respectfully submitted,

Date: January 20, 2004



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9. APPENDIX I

THE REJECTED CLAIMS

Claims 1- 65 (cancelled)

66. A layered granule having a single seed particle, the layers comprising:
    a) a protein matrix layered over the seed particle wherein said matrix comprises a protein solution or slurry to which is added a combination of a sugar or sugar alcohol and a polysaccharide structuring agent; and
    b) an outer barrier layer or coating.

67. The granule of claim 66, wherein the protein solution or slurry is mixed together with a sugar.

68. The granule of claim 67, wherein the sugar is selected from the group consisting of glucose, fructose, raffinose, maltose, lactose, trehalose, and sucrose.

69. The granule of claim 68, wherein the sugar is sucrose.

70. (Withdrawn)

71. (Withdrawn)

72. The granule of claim 66, wherein the polysaccharide structuring agent is selected from the group consisting of starch, modified starch, cellulose, modified cellulose, carrageenan, gum arabic, xanthan gum, locust bean gum, and guar gum.

73. The granule of claim 72, wherein the polysaccharide is a starch or modified starch.

74. The granule of claim 66, wherein the protein solution or slurry is an enzyme.

75. The granule of claim 74, wherein said enzyme is selected from the group consisting of proteases, amylases, lipases, and cellulases.

76. The granule of claim 74, wherein the enzyme is mixed together with a sugar.

77. (Withdrawn)

78. The granule of claim 66 having a coating layered over the protein matrix.

79. The granule of claim 78, wherein the coating is selected from the group consisting of polyvinyl alcohol, polyvinyl pyrrolidone, cellulose derivative, polyethylene glycol, polyethylene oxide, chitosan, gum arabic, xanthan and carrageenan.

80. The granule of claim 79, wherein the coating layer comprises a cellulose derivative.

81. The granule of claim 80, wherein said cellulose derivative is selected from the group consisting of methylcellulose, hydroxypropyl methylcellulose, hydroxycellulose, ethylcellulose, carboxymethyl cellulose, and hydroxypropyl cellulose.

82. The granule of claim 66 further comprising a synthetic polymer selected from the group consisting of polyethylene oxide, polyvinyl alcohol, polyvinyl pyrrolidone, polyethylene glycol and polyethylene oxide/polypropylene oxide.

83. A layered enzyme granule having a single seed particle, the layers comprising:

a) an enzyme matrix layered over the seed particle wherein said matrix is 20 to 80% by weight of the layered granule and comprises an enzyme solution or slurry mixed together with an added combination of a sugar and a polysaccharide structuring agent, said enzyme solution or slurry selected from the group consisting of proteases, amylases, lipases and cellulases and said polysaccharide structuring agent selected from the group consisting of starch, modified starch, cellulose, modified cellulose, carrageenan, gum Arabic, xanthan gum, locust bean gum, and guar gum; and

b) an outer barrier or coating.

84. The enzyme granule of claim 83 further comprising a coating layered over the enzyme matrix.

85. The granule of claim 83, wherein said sugar is selected from the group consisting of glucose, fructose, raffinose, maltose, lactose, trehalose and sucrose.

86. The granule of claim 85, wherein the sugar is sucrose and the polysaccharide is starch or modified starch.

87. The granule of claim 83, wherein the enzyme solution or slurry is a protease.

88. The granule of claim 83, wherein the enzyme solution or slurry is a cellulase.

89. The granule of claim 66 wherein a ratio of the sugar or sugar alcohol to the polysaccharide structuring agent in the protein matrix is 0.1 to 90% by weight of the protein matrix.

90. The granule of claim 83 wherein a ratio of the sugar to the polysaccharide structuring agent in the enzyme matrix is 0.1 to 90% by weight of the enzyme matrix.

91. The granule of claim 66 having a barrier layer over the protein matrix layer.

92. The granule of claim 91 wherein the barrier layer is selected from the group consisting of inorganic salts, organic salts, and the combination of the sugar or sugar alcohol and structuring agent.

93. The granule of claim 66 wherein the barrier layer is an inorganic salt.

94. The granule of claim 66 wherein the barrier layer is magnesium sulfate.

95. The granule of claim 83 having a barrier layer over the enzyme matrix layer.

96. The granule of claim 95 wherein the barrier layer is selected from the group consisting of inorganic salts, organic salts, and the combination of the sugar and structuring agent.

97. The granule of claim 83 wherein the barrier layer is an inorganic salt.

98. The granule of claim 83 wherein the barrier layer is magnesium sulfate.

99. The granule of claim 66 having an outer barrier layer over the protein layer and a coating over the barrier layer.

100. The granule of claim 83 having an outer barrier layer over the protein layer and a coating over the barrier layer.

101. The granule of claim 83 wherein the enzyme solution or slurry is an amylase.

102. The granule of claim 66 wherein the barrier layer is an inorganic salt and titanium dioxide.

103. The granule of claim 83 wherein the barrier layer is an inorganic salt and titanium dioxide.

104. The granule of claim 66 having a barrier layer and a coating.

105. The granule of claim 83 having a barrier layer and a coating.

106. A layered granule comprising:

a) a single seed particle;

b) an enzyme matrix layered over the seed particle wherein said matrix includes at least one enzyme solution or slurry mixed together with an added combination of a sugar and at least one polysaccharide structuring agent and constitutes from about 20 to 80% by weight of the layered granule;

c) a barrier salt layered over the enzyme matrix layer; and

d) an outer coating over the barrier layer.

107. The layered granule of claim 106 wherein the sugar is sucrose; the polysaccharide structuring agent is one or more starches, the barrier salt is magnesium sulfate, and the outer coating is selected from one or more of polyvinyl alcohol, titanium dioxide and a surfactant.